made in accordance with the claimed invention as diagnostic aids. This rejection is traversed.

In making this rejection, the examiner stated that Applicants do not appear to have traversed previously this ground of rejection. Applicants respectfully disagree with this statement. In the Amendment After Final filed in connection with the parent of this application, Applicants submitted a Declaration Pursuant to 37 C.F.R. § 1.132 by Dr. Alan Lewis. In that declaration, Dr. Lewis explained that persons of ordinary skill in the art would be able to use the antibodies of the present invention as diagnostic agents without the need for detailed instructions in the application or undue experimentation. A copy of that declaration is submitted herewith.

Claims 1-2, 4-5, 7-10 and 12-14 were rejected under 35 U.S.C. § 102(b) as anticipated by, or under 35 U.S.C. § 103 as obvious over, Gillies et al. Gillies et al. were said to teach methods for the production of human (primate) antibodies from cDNA libraries, as well as transfected cell lines, transfecting vectors and human (primate) antibodies. These rejections are traversed.

Gillies et al. do not anticipate the claims of the present application. Gillies et al. teach that the light chain of an antibody can be obtained from cDNA encoding both the variable and constant regions of the antibody chain. Gillies et al. teach, however, obtaining the heavy chain of an antibody by expressing a

DNA sequence comprising cDNA encoding the variable region linked to genomic DNA encoding the constant region. The claims of this application, as amended, specify that the entire cDNA sequence encoding each of the light and heavy chains of the antibody are cloned and inserted into a vector. Gillies et al. do not teach this.

The examiner noted in the Office Action that the amendments set forth above would not be sufficient to obviate the § 103 rejection, as methods of inserting complete cDNA sequences into expression vectors were known in the art prior to the Applicants' invention. Of record in connection with this application is a declaration by Dr. Alan Lewis, one of the inventors of the invention disclosed and claimed in the present application. This declaration was filed with a Preliminary Amendment which crossed in the mail with the outstanding Office Action and thus has not been considered by the examiner. In this declaration, Dr. Lewis explains in detail why it was not obvious in view of the art cited by the examiner to make recombinant antibodies according to the Applicants' method. In his declaration, Dr. Lewis explains that at the time of the present invention it was believed necessary to remove the 3' untranslated region of the DNA sequence encoding each chain of the desired antibody prior to expressing the antibody. For the sequence encoding the light chain of the antibody, a restriction enzyme could be used in a partial digest to remove the 3' untranslated sequence in the constant region DNA. For the constant region of the heavy chain,

however, no restriction enzyme recognition sites exist to allow cleavage of the sequence to remove the 3′ untranslated sequence. As a result, Gillies et al. grafted genomic DNA encoding the heavy chain constant region to cDNA encoding the variable region of the heavy chain of the antibody of interest. Accordingly, at the time of the present invention, it was believed by those of skill in the art that in order to produce a recombinant antibody it was necessary to remove the 3′ untranslated region of the sequence encoding each of the heavy and light chains and that, for the heavy chain, this could only be achieved by removing the sequence encoding the constant region and replacing it with genomic DNA of the appropriate Ig class. In contrast, the present inventors surprisingly found that the entire cDNA, including the polyadenylation sequence and preceding untranslated region, was suitable for expression of both the heavy and light chains of an antibody.

Claims 3 and 6 stand rejected under 35 U.S.C. § 103 as unpatentable over Gillies et al. in view of Foung et al. and Ehrlich et al. This rejection is traversed.

The discussion of the inadequacies of the Gillies et al. reference above is equally applicable to this rejection. The teachings of the secondary references cited by the examiner are not sufficient to overcome these deficiencies. Neither Foung nor Ehrlich et al. teach or suggest any method for producing recombinant antibodies, much less that a recombinant antibody could be produced by obtaining the cDNA encoding the entire

constant and variable regions of each of the heavy and light chain of the antibody, inserting the cDNA into an expression vector under the control of expression signals, transfecting a cell with the expression vector and then culturing the cell under antibody-producing conditions.

Claim 11 stands rejected under 35 U.S.C. § 103 as obvious over Gillies et al. in view of Larrick et al. Again, the deficiencies of the Gillies et al. reference as set forth above, are equally applicable to this rejection. The secondary reference does not compensate for the deficiencies of the primary reference. Gillies et al. teach that it is necessary to use genomic DNA as the source for part of the DNA encoding the constant region of the antibody chain. Larrick et al. do not address this issue. They teach a method of amplifying human monoclonal antibody variable region genes using PCR and a mixture of upstream primers corresponding to the leader sequence and one downstream primer designed from the conserved nucleotide sequence of the constant region. The reference does not teach any primers which would enable the amplification and cloning of the entire gene including both the constant and variable regions. The combined teachings of these references do not teach or suggest the method set forth in claim 11 of this application.

Applicants respectfully submit that, in view of the amendments to the claims, the declaration by Dr. Lewis and the